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ctg ( Leu ( 65																240
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gga 1 Gly 1																336
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<301> Davis et al.
<302> Histidine to Alanine mutants of Human Dihydroorota
<303> Biochem. Pharmacol. (1997)
<304> 54
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Val	Ser	Arg	Pro 260	Ala	Gly	Leu	Gln	Gly 265	Ala	Leu	Arg	Ser	Glu 270	Thr	Gly	
Gly	Leu	Ser 275	Gly	Lys	Pro	Leu	Arg 280	Asp	Leu	Ser	Thr	Gln 285	Thr	Ile	Arg	
Glu	Met 290	Tyr	Ala	Leu	Thr	Gln 295		Arg	Val	Pro	Ile 300		Gly	Val	Gly	
Gly 305		Ser	Ser	Gly	Gln 310		Ala	Leu	Glu	Lys 315		Arg	Ala	Gly	Ala 320	
	Leu	Val	Gln			Thr	Ala	Leu			Trp	Gly	Pro			
Val	Gly	Lys		325 Lys	Arg	Glu	Leu		330 Ala	Leu	Leu	Lys		335 Gln	Gly	
Phe	Gly	Gly 355	340 Val	Thr	Asp	Ala	Ile 360	345 Gly	Ala	Asp	His	Arg 365	350 Arg			
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		ggt Gly														96
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		gcc Ala														192
		cgg Arg														240
		ctg Leu														288
		tac Tyr														336
		gcg Ala 115														384

			cat His													4:	32
			gag Glu													43	80
			ctg Leu													5:	28
			gcc Ala 180													5'	76
			ccg Pro													62	24
			cgg Arg													6′	72
gct Ala 225	atc Ile	ttg Leu	gag Glu	caa Gln	cga Arg 230	gta Val	cgc Arg	gat Asp	ttt Phe	gcc Ala 235	tac Tyr	gca Ala	aac Asn	gga Gly	ttt Phe 240	72	20
	_		gat Asp		_	_	_	_	_	_	_		_	_		76	68
			ggt Gly 260													83	16
			aag Lys													86	64
gac Asp	tat Tyr 290	gtg Val	tat Tyr	tgc Cys	gtg Val	gac Asp 295	cgt Arg	gtg Val	gcc Ala	aaa Lys	tac Tyr 300	gct Ala	gat Asp	att Ile	ctt Leu	91	12
	Val		gta Val	Ser		Pro			Pro		Leu					96	60
_			ccg Pro			_		_	_	_	_	_			_	100	80
			aac Asn 340													105	56
			gac Asp													110	04
cga Arg	gca Ala	tcc Ser	ggt Gly	gtc Val	gac Asp	gga Gly	gtg Val	att Ile	gtc Val	gga Gly	aac Asn	aca Thr	aca Thr	aac Asn	cgt Arg	115	52

370		375		380		
cgc ccc gac Arg Pro Asp 385	c cct ata ccc Pro Ile Pro 390	caa ggt tac Gln Gly Tyr	c act ctt r Thr Leu 395	ccg gcc aag Pro Ala Lys	JJJ	200
gca acg ttg Ala Thr Leu	g aaa gaa acc 1 Lys Glu Thr 405	ggc ggg tat Gly Gly Tyr	t tca ggt r Ser Gly 410	cca cag ctg Pro Gln Leu	ttc gat 12 Phe Asp 415	248
	g gcc ctt gtg Ala Leu Val 420		r Arg Ser		2-2 2-2	296
tcg gaa acg Ser Glu Thr 435	g gcc gga tcc Ala Gly Ser	gcc aag gat Ala Lys Asp 440	t tca gca p Ser Ala	gcg acc ata Ala Thr Ile 445	gcg caa 13 Ala Gln	344
aca gag cca Thr Glu Pro 450	a ggc tcg gaa o Gly Ser Glu	aac gtt cct Asn Val Pro 455	t cct gtg o Pro Val	gaa gcg cca Glu Ala Pro 460		392
ctg ccg cgc Leu Pro Arc 465	e aaa gtt atc g Lys Val Ile 470	ttc gct tcg Phe Ala Ser	g ggt ggt r Gly Gly 475	atc acc aac Ile Thr Asn		440
cag gct cac Gln Ala His	gct gtt tta Ala Val Leu 485	gac aca ggg Asp Thr Gl	g gca tct y Ala Ser 490	gtt gcc atg Val Ala Met		488
acc ggt gtg Thr Gly Val	g gtc tat ggt Val Tyr Gly 500	ggc gtc ggc Gly Val Gly 505	y Thr Val	act cga gtg Thr Arg Val 510		536
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<212> PRT

<213> Aspergillus nidulans

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<221> mutation <222> 344

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                                                       175
             165
Ile Gly Pro Ala Ile Val Glu Val Gly Gly Thr Thr Pro Leu Pro Gln
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                                        190
           180
Asp Gly Asn Pro Arg Pro Arg Glu Phe Arg Leu Pro Ser Gln Arg Ala
195 200 205
Met Ile Asn Arg Tyr Gly Leu Asn Ser Lys Gly Ala Asp His Met Ala
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                                           220
Ala Ile Leu Glu Gln Arg Val Arg Asp Phe Ala Tyr Ala Asn Gly Phe
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                  230
Gly Ala Tyr Asp Ala Ala Lys Gln Arg Val Leu Asp Gly Glu Ala Gly
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               245
Val Pro Pro Gly Ser Leu Gln Pro Gly Lys Leu Leu Ala Val Gln Val
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                            265
Ala Lys Asn Lys Ala Thr Pro Asp Gly Asp Ile Glu Ala Ile Lys Arg
275 280 285
Asp Tyr Val Tyr Cys Val Asp Arg Val Ala Lys Tyr Ala Asp Ile Leu
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Val Val Asn Val Ser Ser Pro Asn Thr Pro Gly Leu Arg Asp Leu Gln
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Ala Thr Ala Pro Leu Thr Ala Ile Leu Ser Ala Val Val Gly Ala Ala
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Lys Ser Val Asn Arg Lys Thr Lys Pro Tyr Val Met Val Lys Val Ser
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Pro Asp Glu Asp Ser Asp Glu Gln Val Ser Gly Ile Cys Asp Ala Val
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Arg Ala Ser Gly Val Asp Gly Val Ile Val Gly Asn Thr Thr Asn Arg
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Arg Pro Asp Pro Ile Pro Gln Gly Tyr Thr Leu Pro Ala Lys Glu Gln
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385
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Ala Thr Leu Lys Glu Thr Gly Gly Tyr Ser Gly Pro Gln Leu Phe Asp
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Arg Thr Val Ala Leu Val Ala Arg Tyr Arg Ser Met Leu Asp Ala Glu
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Ser Glu Thr Ala Gly Ser Ala Lys Asp Ser Ala Ala Thr Ile Ala Gln
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Thr Glu Pro Gly Ser Glu Asn Val Pro Pro Val Glu Ala Pro Ser Gly
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Leu Pro Arg Lys Val Ile Phe Ala Ser Gly Gly Ile Thr Asn Gly Lys
465 470 475 480
Gln Ala His Ala Val Leu Asp Thr Gly Ala Ser Val Ala Met Met Tyr
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ctg Leu	ggt Gly	ggt Gly	tgt Cys 20	cgc Arg	cgt Arg	ctc Leu	cca Pro	cta Leu 25	acc Thr	tgc Cys	aga Arg	caa Gln	ctt Leu 30	cga Arg	ttc Phe	96
gcc Ala	tcc Ser	gac Asp 35	agc Ser	gga Gly	gcc Ala	gca Ala	gcg Ala 40	gca Ala	act Thr	aca Thr	aaa Lys	gca Ala 45	acg Thr	gcc Ala	gaa Glu	144
tca Ser	gca Ala 50	gcc Ala	gag Glu	tca Ser	gct Ala	agt Ser 55	ata Ile	aac Asn	gtc Val	aaa Lys	gag Glu 60	gca Ala	ccc Pro	aaa Lys	aag Lys	192
						cgc Arg										240
acg Thr	ctg Leu	ctg Leu	gtt Val	gga Gly 85	tat Tyr	gtc Val	tac Tyr	gly aaa	acg Thr 90	gac Asp	acc Thr	cgg Arg	gcg Ala	agt Ser 95	gtg Val	288
cat His	cgg Arg	tac Tyr	ggt Gly 100	gtt Val	gtg Val	ccg Pro	ctg Leu	att Ile 105	aga Arg	gca Ala	ttg Leu	tat Tyr	cct Pro 110	gat Asp	gcg Ala	336
gaa Glu	gat Asp	gtg Val 115	cat His	cat His	att Ile	ggt Gly	gtc Val 120	gat Asp	act Thr	tta Leu	aag Lys	atg Met 125	ctg Leu	tat Tyr	aag Lys	384
tat Tyr	ggt Gly 130	ctg Leu	cat His	cca Pro	agg Arg	gaa Glu 135	cgg Arg	ejà aaa	gat Asp	ccg Pro	gat Asp 140	gga Gly	gat Asp	glà aaa	gcg Ala	432
ctg Leu 145	gcg Ala	aca Thr	gag Glu	gtc Val	ttt Phe 150	gly aaa	tat Tyr	aca Thr	ctg Leu	tca Ser 155	aac Asn	cca Pro	att Ile	ggc Gly	ata Ile 160	480
tcg Ser	ggc Gly	ggc Gly	ctg Leu	gac Asp 165	aag Lys	cat His	gct Ala	gag Glu	atc Ile 170	cct Pro	gat Asp	ccg Pro	ctg Leu	ttc Phe 175	gcg Ala	528
atc Ile	ggt Gly	cct Pro	gcc Ala 180	att Ile	gtc Val	gaa Glu	gtc Val	999 Gly 185	ggt Gly	acg Thr	aca Thr	ccc Pro	tta Leu 190	cca Pro	cag Gln	576
gat Asp	ggt Gly	aac Asn 195	ccg Pro	cgt Arg	cct Pro	cgc Arg	gta Val 200	ttc Phe	cga Arg	ctt Leu	cca Pro	tca Ser 205	cag Gln	aga Arg	gcg Ala	624
atg Met	ata Ile 210	aac Asn	cgg Arg	tac Tyr	ggc Gly	ctc Leu 215	aac Asn	tcc Ser	aaa Lys	ggc Gly	gca Ala 220	gat Asp	cac His	atg Met	gca Ala	672
gct Ala 225	atc Ile	ttg Leu	gag Glu	caa Gln	cga Arg 230	gta Val	cgc Arg	gat Asp	ttt Phe	gcc Ala 235	tac Tyr	gca Ala	aac Asn	gga Gly	ttt Phe 240	720

Gly ggg	gca Ala	tac Tyr	gat Asp	gcg Ala 245	gct Ala	aag Lys	cag Gln	cgt Arg	gta Val 250	ttg Leu	gac Asp	ggc Gly	gaa Glu	gct Ala 255	ggt Gly	768
gtg Val	cca Pro	cca Pro	ggt Gly 260	agt Ser	ctt Leu	cag Gln	cct Pro	ggt Gly 265	aag Lys	ctt Leu	tta Leu	gct Ala	gtc Val 270	caa Gln	gtg Val	816
gca Ala	aag Lys	aac Asn 275	aag Lys	gcc Ala	act Thr	cct Pro	gac Asp 280	ggc Gly	gac Asp	att Ile	gaa Glu	gcc Ala 285	atc Ile	aag Lys	cgc Arg	864
gac Asp	tat Tyr 290	gtg Val	tat Tyr	tgc Cys	gtg Val	gac Asp 295	cgt Arg	gtg Val	gcc Ala	aaa Lys	tac Tyr 300	gct Ala	gat Asp	att Ile	ctt Leu	912
gtt Val 305	gtg Val	aat Asn	gta Val	tcg Ser	agc Ser 310	ccc Pro	aac Asn	aca Thr	ccc Pro	ggt Gly 315	ctc Leu	cgt Arg	gac Asp	ctt Leu	caa Gln 320	960
gcc Ala	act Thr	gcc Ala	ccg Pro	ctc Leu 325	aca Thr	gct Ala	atc Ile	ttg Leu	agt Ser 330	gct Ala	gtc Val	gtt Val	ggc Gly	gcg Ala 335	gca Ala	1008
aag Lys	agc Ser	gtg Val	aac Asn 340	cgc Arg	aag Lys	acc Thr	aaa Lys	cca Pro 345	tat Tyr	gtt Val	atg Met	gtc Val	aag Lys 350	gtc Val	agt Ser	1056
ccg Pro	gat Asp	gaa Glu 355	gac Asp	tca Ser	gat Asp	gaa Glu	caa Gln 360	gtc Val	tct Ser	ggt Gly	atc Ile	tgc Cys 365	gac Asp	gcc Ala	gtc Val	1104
cga Arg	gca Ala 370	tcc Ser	ggt Gly	gtc Val	gac Asp	gga Gly 375	gtg Val	att Ile	gtc Val	gga Gly	aac Asn 380	aca Thr	aca Thr	aac Asn	cgt Arg	1152
cgc Arg 385	ccc Pro	gac Asp	cct Pro	ata Ile	ccc Pro 390	caa Gln	ggt Gly	tac Tyr	act Thr	ctt Leu 395	ccg Pro	gcc Ala	aag Lys	gag Glu	cag Gln 400	1200
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ctg Leu 465	ccg Pro	cgc Arg	aaa Lys	gtt Val	atc Ile 470	ttc Phe	gct Ala	tcg Ser	ggt Gly	ggt Gly 475	atc Ile	acc Thr	aac Asn	Gly aaa	aag Lys 480	1440
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Thr Gly Val Val Tyr Gly Gly Val Gly Thr Val Thr Arg Val Lys Gln
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Ala Ser Asp Ser Gly Ala Ala Ala Ala Thr Thr Lys Ala Thr Ala Glu
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Ser Ala Ala Glu Ser Ala Ser Ile Asn Val Lys Glu Ala Pro Lys Lys
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Thr Leu Leu Val Gly Tyr Val Tyr Gly Thr Asp Thr Arg Ala Ser Val
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His Arg Tyr Gly Val Val Pro Leu Ile Arg Ala Leu Tyr Pro Asp Ala
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Glu Asp Val His His Ile Gly Val Asp Thr Leu Lys Met Leu Tyr Lys
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Tyr Gly Leu His Pro Arg Glu Arg Gly Asp Pro Asp Gly Asp Gly Ala
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Leu Ala Thr Glu Val Phe Gly Tyr Thr Leu Ser Asn Pro Ile Gly Ile
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                     150
Ser Gly Gly Leu Asp Lys His Ala Glu Ile Pro Asp Pro Leu Phe Ala
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                                     170
Ile Gly Pro Ala Ile Val Glu Val Gly Gly Thr Thr Pro Leu Pro Gln
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Asp Gly Asn Pro Arg Pro Arg Val Phe Arg Leu Pro Ser Gln Arg Ala
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Met Ile Asn Arg Tyr Gly Leu Asn Ser Lys Gly Ala Asp His Met Ala
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Gly Ala Tyr Asp Ala Ala Lys Gln Arg Val Leu Asp Gly Glu Ala Gly
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Ala Lys Asn Lys Ala Thr Pro Asp Gly Asp Ile Glu Ala Ile Lys Arg
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Asp Tyr Val Tyr Cys Val Asp Arg Val Ala Lys Tyr Ala Asp Ile Leu
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Val Val Asn Val Ser Ser Pro Asn Thr Pro Gly Leu Arg Asp Leu Gln
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Ala Thr Ala Pro Leu Thr Ala Ile Leu Ser Ala Val Val Gly Ala Ala
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330

Lys Ser Val Asn Arg Lys Thr Lys Pro Tyr Val Met Val Lys Val Ser 345

325

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                                                380
Arg Pro Asp Pro Ile Pro Gln Gly Tyr Thr Leu Pro Ala Lys Glu Gln
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                                           395
385
Ala Thr Leu Lys Glu Thr Gly Gly Tyr Ser Gly Pro Gln Leu Phe Asp
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                                       410
                                                             415
Arg Thr Val Ala Leu Val Ala Arg Tyr Arg Ser Met Leu Asp Ala Glu
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Ser Glu Thr Ala Gly Ser Ala Lys Asp Ser Ala Ala Thr Ile Ala Gln
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Thr Glu Pro Gly Ser Glu Asn Val Pro Pro Val Glu Ala Pro Ser Gly
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Gln Ala His Ala Val Leu Asp Thr Gly Ala Ser Val Ala Met Met Tyr
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Asp Asp Gly Leu Thr Ala Gln Gln Leu Phe Asn Cys Gly Asp Gly Leu
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Thr Tyr Asn Asp Phe Leu Ile Leu Pro Gly Tyr Ile Asp Phe Thr Ala
gat cag gtg gac ttg acg tct gct cta act aag aag att aca cta aag
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Asp Gln Val Asp Leu Thr Ser Ala Leu Thr Lys Lys Ile Thr Leu Lys
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                                                                           348
tgc aca cct gaa ttc cag gcc aat gaa gtt cgg aaa gtg aag aaa tac
Cys Thr Pro Glu Phe Gln Ala Asn Glu Val Arg Lys Val Lys Lys Tyr
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ttg Leu 175	gaa Glu	gag Glu	atc Ile	atg Met	act Thr 180	aag Lys	agg Arg	gaa Glu	gat Asp	ttg Leu 185	gtg Val	gtc Val	gcc Ala	cct Pro	gcc Ala 190		636
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								aag Lys								1	L020
								agt Ser								-	1068
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ttc Phe	agt Ser	gaa Glu	gct Ala	gac Asp 435	aaa Lys	atc Ile	aaa Lys	gtg Val	gcc Ala 440	caa Gln	gga Gly	gtt Val	tca Ser	ggg Gly 445	gca Ala	1404
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	)> 3( Ala		Tvr	Leu	Ile	Ser	Glv	Gly	Thr	Ser	Tyr	Val	Pro	Asp	Asp	
1		-	_	5			_	Asn	10				Leu	15 Thr		
Asn	Asp		20 Leu	Ile	Leu	Pro	Gly	25 Tyr	Ile	Asp	Phe	Thr 45	30 Ala	Asp	Gln	
Val	Asp 50	35 Leu	Thr	Ser	Ala	Leu 55		Lys	Lys	Ile	Thr 60		Lys	Thr	Pro	
65	Val				70	Asp				75	Ala			Ala	80	
λla	Mot	7.7.5	T. 211	Thr	C137	G137	Tle	C137	Dhe	Tle	His	His	Agn	Cvs	Thr	

Ala Met Ala Leu Thr Gly Gly Ile Gly Phe Ile His His Asn Cys Thr

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Asp Val Phe Glu Ala Lys Ala Arg His Gly Phe Cys Gly Ile Pro Ile
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Thr Asp Thr Gly Arg Met Gly Ser Arg Leu Val Gly Ile Ile Ser Ser 145 150 155 160
Arg Asp Ile Asp Phe Leu Lys Glu Glu Glu His Asp Arg Phe Leu Glu
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Glu Ile Met Thr Lys Arg Glu Asp Leu Val Val Ala Pro Ala Gly Val
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Thr Leu Lys Glu Ala Asn Glu Ile Leu Gln Arg Ser Lys Lys Gly Lys
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Thr Asp Leu Lys Lys Asn Arg Asp Tyr Pro Leu Ala Ser Lys Asp Ala
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Lys Lys Gln Leu Cys Gly Ala Ala Ile Gly Thr His Glu Asp Asp
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Leu Phe
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<sup>&</sup>lt;211> 1707

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gac gac ggg ctc aca gcg cag cag ctc ttc aac tgc ggg gac ggc ctc Asp Asp Gly Leu Thr Ala Gln Gln Leu Phe Asn Cys Gly Asp Gly Leu 15 20 25 30	156
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tgc aca cct gaa ttc cag gcc aat gaa gtt cgg aaa gtg aag aaa tac Cys Thr Pro Glu Phe Gln Ala Asn Glu Val Arg Lys Val Lys Lys Tyr 95 100 105 110	396
gaa cag gga ttc atc act gac ccc gtg gtc ctt agc ccc aag gat cgt Glu Gln Gly Phe Ile Thr Asp Pro Val Val Leu Ser Pro Lys Asp Arg 115 120 125	444
gta cgc gat gtt ttt gag gcc aaa gcc agg cat ggc ttc tgt ggt atc Val Arg Asp Val Phe Glu Ala Lys Ala Arg His Gly Phe Cys Gly Ile 130 135 140	492
ccc atc aca gat aca ggc cgg atg ggg agt cga ttg gtg ggc atc atc Pro Ile Thr Asp Thr Gly Arg Met Gly Ser Arg Leu Val Gly Ile Ile 145 150 155	540
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Gly Val Thr Leu Lys		Glu Ile Leu Gln Arg	Ser Lys Lys
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gat gcc aag aag ca Asp Ala Lys Lys Gli 240	a ctg ctg tgt o n Leu Leu Cys ( 245	ggg gca gcc att ggc Gly Ala Ala Ile Gly 250	act cat gag 828 Thr His Glu
gat gac aag tat ag	g ctg gac tta o	ctg gcc ctt gct ggt	gtg gat gta 876
Asp Asp Lys Tyr Ar	g Leu Asp Leu 1	Leu Ala Leu Ala Gly	Val Asp Val
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Val Val Leu Asp Se		Asn Ser Ile Phe Gln	Ile Asn Met
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Ile Lys Tyr Ile Ly		Pro Ser Leu Gln Val	Ile Gly Gly
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gat gct ttg cga gt Asp Ala Leu Arg Va 320	c ggc atg gga l Gly Met Gly : 325	agt ggt tcc atc tgc Ser Gly Ser Ile Cys 330	atc atc cag 1068 Ile Ile Gln
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Glu Val Leu Ala Cy	s Gly Arg Pro	Gln Ala Thr Ala Val	Tyr Lys Val
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Ile Gln Asn Val Gl		Lys Ala Leu Ala Leu	Gly Ala Ser
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gag tac ttc ttc tc Glu Tyr Phe Phe Se 400	a gat ggg atc r Asp Gly Ile 405	cgg ctg aag aaa tac Arg Leu Lys Lys Tyr 410	cga ggt atg 1308 Arg Gly Met
ggt tct ctt gat gc	c atg gac aaa	cat ctc agc agc cag	aac cga tac 1356
Gly Ser Leu Asp Al	a Met Asp Lys	His Leu Ser Ser Gln	Asn Arg Tyr
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tcc tct gct cag gtg gaa ggt ggc gtc cac agc ctc cat tcg tac gag Ser Ser Ala Gln Val Glu Gly Gly Val His Ser Leu His Ser Tyr Glu 495 500 505	1596
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100 105 110  Gly Phe Ile Thr Asp Pro Val Val Leu Ser Pro Lys Asp Arg Val Arg 115 120 125  Asp Val Phe Glu Ala Lys Ala Arg His Gly Phe Cys Gly Ile Pro Ile	
Gly Phe Ile Thr Asp Pro Val Val Leu Ser Pro Lys Asp Arg Val Arg 115  Asp Val Phe Glu Ala Lys Ala Arg His Gly Phe Cys Gly Ile Pro Ile 130  Thr Asp Thr Gly Arg Met Gly Ser Arg Leu Val Gly Ile Ile Ser Ser	
Gly Phe Ile Thr Asp Pro Val Val Leu Ser Pro Lys Asp Arg Val Arg  115  Asp Val Phe Glu Ala Lys Ala Arg His Gly Phe Cys Gly Ile Pro Ile  130  Thr Asp Thr Gly Arg Met Gly Ser Arg Leu Val Gly Ile Ile Ser Ser  145  Arg Asp Ile Asp Phe Leu Lys Glu Glu Glu His Asp Arg Phe Leu Glu	
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Gly Phe Ile Thr Asp Pro Val Val Leu Ser Pro Lys Asp Arg Val Arg 115  Asp Val Phe Glu Ala Lys Ala Arg His Gly Phe Cys Gly Ile Pro Ile 130  Thr Asp Thr Gly Arg Met Gly Ser Arg Leu Val Gly Ile Ile Ser Ser 145  Arg Asp Ile Asp Phe Leu Lys Glu Glu Glu His Asp Arg Phe Leu Glu 165  Glu Ile Met Thr Lys Arg Glu Asp Leu Val Val Ala Pro Ala Gly Val 180  Thr Leu Lys Glu Ala Asn Glu Ile Leu Gln Arg Ser Lys Lys Gly Lys	
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Leu	Arg			325					330					335	
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	Val 370					375					380				
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_	Lys 450					455					460				
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based cloning of hIMPDH type II cDNA
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of hIMPDH type II cDNA
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